UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/830,839	02/19/2002	Ajit Lalvani	077529.0111	3551

21003 7590 01/16/2009

BAKER BOTTS L.L.P.
30 ROCKEFELLER PLAZA
44TH FLOOR
NEW YORK, NY 10112-4498

EXAMINER	
MINNIFIELD, NITA M	

ART UNIT	PAPER NUMBER
1645	

NOTIFICATION DATE	DELIVERY MODE
01/16/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

DLNYDOCKET@BAKERBOTTS.COM

Office Action Summary	Application No.	Applicant(s)	
	09/830,839	LALVANI ET AL.	
	Examiner	Art Unit	
	N. M. Minnifield	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 September 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *88-111* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *88-111* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

1. Applicants' amendment filed September 28, 2007 is acknowledged and has been entered. Claims 1-87 have been canceled. New claims 88-111 have been added. Claims 88-111 are now pending in the present application. All rejections have been withdrawn in view of Applicants' amendment to the claims and/or comments, with the exception of those discussed below.

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 88-111 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

In 1999, the United States Patent and Trademark Office ("USPTO") published training materials regarding the examination of patent applications under the written description requirement of 35 U.S.C. § 112, first paragraph. (See http://www.uspto.gov/web/offices/pac/writtendesc.pdf). Since that time, the case law and technology have developed in such a way as to necessitate a revision of the 1999 training materials. Consequently, this revision was created to supersede

and replace the 1999 training materials. To the extent that any conflict exists between the 1999 training materials and the present materials, the present materials control. The claims have been evaluated with regard to written description based on the Written Description Guidelines and Training Materials published in 2008.

Claim 88, for example, is directed to a method of diagnosing infection in a human patient by, or exposure of a human patient to, a mycobacterium that expresses ESAT-6, which method comprises the steps of: (i) contacting a population of T cells from the patient with a high sensitivity panel of eight peptides, in which each peptide has a sequence at least 90% identical to one of SEQ ID NOS: 1 to 8 or has an end terminal deletion of one of SEQ ID NOS: 1 to 8 such that each of SEQ ID NOS: 1 to 8 is represented in the panel, wherein each peptide in the panel retains the ability to be recognized by T cells of a T cell population which recognize a peptide having a corresponding exact sequence of SEQ ID NOS: 1 to 8, and (ii) determining *in vitro* whether T cells of the T cell population show a recognition response to the peptides by detecting IFN-γ secretion from the T cells. Claim 89, for example, is directed to the method of claim 88, wherein the panel further comprises one or more peptides selected from the group consisting of a peptide having a sequence at least 90% identical to SEQ ID NO: 9 or having an end terminal deletion of SEQ ID NO: 9, and which retains the ability to be recognized by T cells of a T cell population which recognize a peptide having a sequence of SEQ ID NO: 9; a peptide having a sequence at least 90% identical to SEQ ID NO: 10 or having an end terminal deletion of SEQ ID NO: 10, and which retains the ability to be recognized by T cells of a T cell population which recognize a peptide having a sequence of SEQ ID NO: 10; and a peptide having a sequence at least 90% identical to SEQ ID NO: 11 or having

an end terminal deletion of SEQ ID NO: 11, and which retains the ability to be recognized by T cells of a T cell population which recognize a peptide having a sequence of SEQ ID NO: 11. Additional claims are directed to kits and compositions comprising these peptides.

The specification has not described "a sequence at least 90% identical to one of SEQ ID NOS: 1 to 8 or has an end terminal deletion of one of SEQ ID NOS: 1 to 8…wherein each peptide in the panel retains the ability to be recognized by T cells of a T cell population which recognize a peptide having a corresponding exact sequence of SEQ ID NOS: 1 to 8…" The specification does not teach the structure of the vast genus of peptides having the recited "sequence at least 90% identical to one of SEQ ID NOS: 1 to 8 or has an end terminal deletion of one of SEQ ID NOS: 1 to 8…wherein each peptide in the panel retains the ability to be recognized by T cells of a T cell population which recognize a peptide having a corresponding exact sequence of SEQ ID NOS: 1 to 8. The recitation of the "at least 90%" is viewed as a fragment or variant, something less than the whole peptide. The recitation of "end terminal deletion of one of SEQ ID NOS: 1 to 8", for example, is viewed as a fragment or variant as well. The same is true for peptides SEQ ID NOS: 9-11. What is the structure of the peptide that is "a sequence at least 90%" of each of the eleven peptides? How much of the peptide at the terminal end is deleted? Which end, 5' or 3', is deleted or can both terminal ends have a deletion? The written description problem exists for each of the claimed peptides, SEQ ID NOS: 1-11. The structure of these peptides cannot be envisioned, aside from the peptide having the exact sequence of SEQ ID NOS: 1-11.

To fulfill the written description requirements set forth under 35 USC § 112, first paragraph, the specification must describe at least a substantial number of the

members of the claimed genus, or alternatively describe a representative member of the claimed genus, which shares a particularly defining feature common to at least a substantial number of the members of the claimed genus, which would enable the skilled artisan to immediately recognize and distinguish its members from others, so as to reasonably convey to the skilled artisan that Applicant has possession the claimed invention. Applicants have not described the genus of claimed peptides such that the specification might reasonably convey to the skilled artisan that Applicants had possession of the claimed invention at the time the application was filed.

The purpose of the "written description" requirement is broader than to merely explain how to "make and use"; the applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the "written description" inquiry, whatever is now claimed. See Vas-Cath, Inc. v. Mahurkar, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Federal Circuit, 1991). Furthermore, the written description provision of 35 USC §112 is severable from its enablement provision; and adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. The Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, paragraph 1, "'Written Description" Requirement (66 FR 1099-1111, January 5, 2001) state, "[p]ossession may be shown in a variety of ways including description of an actual reduction to practice, or by showing the invention was 'ready for patenting' such as by disclosure of drawings or structural chemical formulas that show that the

invention was complete, or by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention" (Id. at 1104). Moreover, because the claims encompass a genus of variant species, an adequate written description of the claimed invention must include sufficient description of at least a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics sufficient to show that Applicant was in possession of the claimed genus. However, factual evidence of an actual reduction to practice has not been disclosed by Applicant in the specification; nor has Applicant shown the invention was "ready for patenting" by disclosure of drawings or structural chemical formulas that show that the invention was complete; nor has Applicant described distinguishing identifying characteristics sufficient to show that Applicant were in possession of the claimed invention at the time the application was filed. The Guidelines further state, "[f]or inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus'" (Id. at 1106); accordingly, it follows that an adequate written description of a genus cannot be achieved in the absence of a disclosure of at least one species within the genus. As evidenced by Greenspan et al *(Nature Biotechnology 7: 936-937, 1999),* defining epitopes is not as easy as it seems. Greenspan et al recommends defining an epitope by the structural characterization of the molecular interface between the antigen and the antibody is necessary to define an "epitope" (page 937, column 2). According to Greenspan et al, an epitope will include residues that make contacts with a ligand, here the antibody, but are energetically neutral, or even destabilizing to binding. Furthermore, an epitope will not include any residue not contacted by

the antibody, even though substitution of such a residue might profoundly affect binding. Chothia et al (THE EMBO JOURNAL, 1986, 5/4:823-26) also teach that there is a limit to how much substitution can be tolerated before the original tertiary structure is lost. Therefore, absent a detailed and particular description of a representative number, or at least a substantial number of the members of the genus of fragments or variants of the eleven peptides, the skilled artisan could not immediately recognize that Applicants were in possession of the claimed genus of peptides at the time of filing.

Therefore, because the art is unpredictable, in accordance with the Written Description Guidelines, the recitation of "a sequence at least 90% identical to one of SEQ ID NOS: 1 to 8 or has an end terminal deletion of one of SEQ ID NOS: 1 to 8 such that each of SEQ ID NOS: 1 to 8 is represented in the panel" is not deemed representative of the claimed genus. The same is true for this recitation reciting SEQ ID NOS: 9-11. The only peptide enabled by the claimed invention under examination in this application, that Applicants were in possession of at the time of filing is sequence SEQ ID NOS: 1-11, not the variants or fragments.

The scope of the claim includes numerous structural variants (i.e. fragments), and the genus is highly variant because a significant number of structural differences between genus members is permitted. The specification does not describe any members of the claimed genus by complete structure. The specification does not describe the structure for deletion variants (i.e. fragments) of each of the peptides of SEQ ID NOS: 1 to 11. The specification does not describe the physical or chemical characteristics for deletion variants (i.e. fragments) of each of the peptides of SEQ ID NOS: 1 to 11. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of

species to describe the genus, and thus, that the applicant was not in possession of the claimed genus. The claimed subject matter is not supported by an adequate written description because a representative number of species has not been described.

There are no drawings or structural formulas disclosed of any of these fragments or variants of the peptide "wherein each peptide in the panel retains the ability to be recognized by T cells of a T cell population which recognize a peptide having a corresponding exact sequence of SEQ ID NOS: 1 to 8" and SEQ ID NOS: 9-11. The recitation of a sequence at least 90% of identical to one of each SEQ ID NOS: 1 to 8, also SEQ ID NOS: 9-11, represents a partial structure. That is, the claimed peptides share at least 90% of the structure of SEQ ID NOS: 1-11, while 10% of the structure can vary or even be deleted. There is no teaching in the specification regarding which 10% of the structure can be varied "wherein each peptide in the panel retains the ability to be recognized by T cells of a T cell population which recognize a peptide having a corresponding exact sequence of SEQ ID NOS: 1 to 8", for example. Consequently, there is no information about which amino acids can vary from SEQ ID NOS: 1-11 in the claimed genus of peptides and still retain the function of "wherein each peptide in the panel retains the ability to be recognized by T cells of a T cell population which recognize a peptide having a corresponding exact sequence of SEQ ID NOS: 1 to 8", for example. Although the disclosure of SEQ ID NOS: 1-11 combined with the knowledge in the art, may put one in possession of peptides that are at least 90% identical to SEQ ID NOS: 1-11, the level of skill and knowledge in the art is such that one of ordinary skill would not be able to identify without further testing which of those peptides having at least 90% identity to SEQ ID NOS: 1-11 (if any)

have the ability to be recognized by T cells of a T cell population which recognize a peptide having a corresponding exact sequence of the peptide (SEQ ID NOS: 1-11). Based on the lack of knowledge and predictability in the art, those of ordinary skill in the art would not conclude that the applicant was in possession of the claimed genus of peptides based on disclosure of the single species of only the exact SEQ ID NOS: 1-11 of the peptides.

Factors to be considered in determining whether undue experimentation is required, are set forth in In re Wands 8 USPQ2d 1400. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and (8) the breadth of the claims.

Applying the above test to the facts of record, it is determined that 1) no declaration under 37 C.F.R. 1.132 or other relevant evidence has been made of record establishing the amount of experimentation necessary, 2) insufficient direction or guidance is presented in the specification with respect to fragments and variants of peptides SEQ ID NOS: 1-11, 3) the relative skill of those in the art is commonly recognized as quite high (post-doctoral level). With regard to (4) the nature of the invention and (5) the state of the prior art, these have been discussed above. One of skill in the art would require guidance, in order to make or use the peptides in the methods, kits and compositions as instantly claimed. The claims are enabled for methods, kits and compositions using the peptides having the exact sequence set forth in SEQ ID NOS: 1-11.

4. No claims are allowed.

5. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to N. M. Minnifield whose telephone number is 571-272-0860. The examiner can normally be reached on M-F (8:00-5:30) Second Friday Off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert B. Mondesi can be reached on 571-272-0956. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR.

Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/N. M. Minnifield/
Primary Examiner, Art Unit 1645
January 13, 2009